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Published
With international search report.

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6 July 2000 (06.07.00)

(54) Title: METHOD FOR SCREENING FOR ANTI-AMYLOIDOGENIC PROPERTIES AND METHOD FOR TREATMENT OF NEURODEGENERATIVE DISEASE

(57) Abstract

In methods for screening treatments for, and treatment of, neurodegenerative diseases, aggregation in neurons of NACP/α–synuclein is measured and expression of a non–amyloidogenic protein is stimulated in order to reduce the level aggregation. For purposes of screening agents for treatment of neurodegenerative disease, oxidative stress in the neuronal cells is stimulated by introducing a mixture of metal–ions and hydrogen peroxide. Examples of appropriate metals include iron, aluminum, and copper. After introduction of the agent under evaluation for stimulation of expression of non–amyloidogenic protein, the effectiveness is measured by testing for a decrease in the level of aggregation of NACP/α–synuclein. In an examplary embodiment, the non–amyloidogenic protein is β–synuclein. The aggregation of NACP/α–synuclein is dependent upon the concentration of metal ions in the neuronal cells. In addition, the presence of chelating agents appears to modulate the build–up of NACP/α–synuclein aggregates which are responsible for synaptic and neuronal dysfunction.

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 99/23134

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Remark: Although claims 1-3 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Intern nal Application No
PCT/US 99/23134

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K38/17 A61K48/00 G01N33/68 A61P25/28

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K C07K G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	MIZUNO YOSHIKUNI ET AL: "Mitochondrial dysfunction in Parkinson's disease." ANNALS OF NEUROLOGY SEPT., 1998, vol. 44, no. 3 SUPPL. 1, 1998, pages S99-S109, XP000891962 ISSN: 0364-5134 the whole document ---	1-10
A	JENNER P. ET AL: "Understanding Cell Death in Parkinson's Disease" ANNALS OF NEUROLOGY SEPT., 1998, vol. 44, no. 3 SUPPL. 1, 1998, pages S99-S109, XP000891957 ISSN: 0364-5134 the whole document ---	1-10

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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Date of the actual completion of the international search	Date of mailing of the international search report
14 April 2000	03/05/2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Moreau, J

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INTERNATIONAL SEARCH REPORT

Intern al Application No
PCT/US 99/23134

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
P,X	EP 0 908 727 A (NEUROPA LIMITED) 14 April 1999 (1999-04-14) claim 19	4
P,X	HASHIMOTO MAKOTO ET AL: "Oxidative stress induces amyloid-like aggregate formation of NACP/alpha-synuclein in vitro." NEUROREPORT MARCH 17, 1999, vol. 10, no. 4, 17 March 1999 (1999-03-17), pages 717-721, XP000891964 ISSN: 0959-4965 the whole document	1-10

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INTERNATIONAL SEARCH REPORT

information on patent family members

Interr .nal Application No
PCT/US 99/23134

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 908727 A	14-04-1999	JP 11239488 A	07-09-1999